General

Guideline Title

ACR Appropriateness Criteria® pre-irradiation evaluation and management of brain metastases.

Bibliographic Source(s)

Lo SS, Gore EM, Bradley JD, Buatti JM, Germano I, Ghafoori AP, Henderson MA, Murad GJ, Patchell RA, Patel SH, Robbins JR, Robins HI, Vassil AD, Wippold FJ II, Yunes MJ, Videtic GM, Expert Panel on Radiation Oncology-Brain Metastases. ACR Appropriateness CriteriaÂ® pre-irradiation evaluation and management of brain metastases [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 9 p. [38 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Gaspar LE, Videtic GM, Gore EM, Bradley JD, Germano I, Ghafoori P, Henderson MA, Lutz ST, McDermott MW, Patchell RA, Patel SH, Robins HI, Vassil AD, Wippold FJ II, Expert Panel on Radiation Oncology-Brain Metastases. ACR Appropriateness Criteria® pre-irradiation evaluation and management of brain metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 6 p. [36 references]

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Pre-Irradiation Evaluation and Management of Brain Metastases

Variant 1: 50-year-old patient with newly diagnosed cancer of any stage and new intracranial signs or symptoms.

Radiologic Procedure	Rating	Comments
MRI head with standard-dose contrast	9	Several members of the panel considered MRI needed only if the exact number of metastases is necessary to make decisions regarding stereotactic radiosurgery or surgery.
CT head with and without contrast	7	Although usually appropriate, one would still need MRI to determine exact number of metastases and determine if patient is a good candidate for stereotactic radiosurgery or surgery. If the CT is negative it is very likely that the radiologist will recommend an MRI since this patient has new intracranial signs or symptoms. CT was thought by many to be indicated only in those patients in whom the

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

Radiologic Procedure	Rating	Comments
		MRI is contraindicated or is unavailable.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 50-year-old patient with newly diagnosed non-small-cell lung cancer with resectable primary and CT evidence of solitary brain metastasis.

Radiologic Procedure	Rating	Comments
MRI head with standard-dose contrast	9	
MRI head with high-dose contrast	6	High dose contrast may not be needed with the availability of new gadolinium-based contrast agents that offer significantly greater diagnostic information and lesion enhancement even at lower doses.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 45-year-old patient with metastatic melanoma and newly diagnosed multiple small supratentorial brain metastases. On treatment with ipilimumab. Mild edema on imaging. No hydrocephalus, neurologic symptoms, or history of seizures.

Treatment	Rating	Comments
Corticosteroids 4 to 8 mg/day	2	Corticosteroids are not absolutely indicated and may interfere with efficacy of ipilimumab.
Corticosteroids 16 mg/day	2	Corticosteroids are not absolutely indicated and may interfere with efficacy of ipilimumab.
Anticonvulsants (prophylactic)	2	In a patient with no history of seizures, the use of prophylactic anticonvulsants is deemed inappropriate.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 50-year-old patient with non–small-cell lung cancer and multiple supratentorial brain metastases. Mild edema on imaging. No hydrocephalus. Mild neurologic symptoms present. No history of seizures.

Treatment	Rating	Comments
Corticosteroids 4 to 8 mg/day	8	
Corticosteroids 16 mg/day	7	Some panel members recommended starting at 16 mg/day and then lowering to 4 to 8 mg after a few days.
Anticonvulsants (prophylactic)	3	In a patient with no history of seizures, the use of prophylactic anticonvulsants is deemed inappropriate.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

The pretreatment evaluation for brain metastases occurs either as part of the staging investigations in a patient who has known systemic cancer, or in a patient who has cerebral or cerebellar symptoms, with or without known systemic cancer. In either case, the evaluation is critical when the presence of brain metastases would alter the overall oncologic management. The patient's clinical symptomatology and overall oncologic picture as

well as the findings on diagnostic imaging of the brain will determine the appropriate treatment for brain metastases. Although brain metastases can arise from virtually any primary cancer, lung and breast are the two most common primary sites of cancer in patients presenting with brain metastases. Other common histologies include melanoma, renal cell carcinoma, and colorectal cancer. The literature regarding pretreatment evaluation and management is dominated by patients with these primary malignancies.

The choice of treatment for brain metastases is often based on patient symptomatology, histology, location, and number of metastases identified on imaging studies. Contrast-enhanced magnetic resonance imaging (MRI) is the imaging test of choice in the patient with suspected brain metastases if surgery or radiosurgery is being considered. Otherwise, computed tomography (CT) with contrast injection is a reasonable study, albeit less sensitive than MRI.

Computed Tomography/Magnetic Resonance Imaging

During the CT era, as many as 50% of patients with brain metastases were found to have a single metastasis. However, it is almost certain that the current percentage is lower, given the increased sensitivity of modern MRI, especially when a volumetric sequence with contiguous thin cuts is included. Current patient data, acquired with modern CT and MRI technology, indicate that about 20% of patients thought to have a single brain metastasis based on CT actually are found to have multiple lesions on MRI. However, CT with contrast remains the best imaging option for investigation of brain metastasis in patients with automatic implantable cardioverter defibrillators or pacemakers. If treatment is to be determined according to the number of brain metastases, MRI with pregadolinium T1- and T2-weighted sequences and post-gadolinium T1-weighted imaging, preferably a thin-cut contiguous volumetric sequence in axial, coronal, and sagittal planes, is recommended.

Fluid-attenuated inversion-recovery (FLAIR) sequences have also been shown to complement, but not replace, contrast-enhanced T1 sequences, and can be correlated with the T1 sequences to determine whether a punctuate contrast-enhanced lesion is a metastatic lesion, which frequently shows signal intensity on FLAIR imaging. Contiguous thin slices without skips are necessary to ensure that small lesions are detected. To reduce costs, a more limited MRI can be done when the intent is merely to determine whether brain metastases are present.

One study demonstrated that a limited MRI scan (T2 axial, proton density axial, and contrast-enhanced T1 sagittal images) could be considered for screening purposes. In 183 patients with newly diagnosed non–small-cell lung cancer (NSCLC), this limited MRI detected brain metastases in approximately 20% of patients. In a historical control group of similar patients with NSCLC who underwent limited MRI only if they had neurological signs or symptoms at the time of diagnosis, 6% were found to have brain metastases. The cost of the limited MRI was approximately 40% of the estimated cost of the normal diagnostic MRI. For a patient with neurologic signs or symptoms, a CT with contrast is reasonable as a first test, but an MRI is required if the decision regarding treatment requires knowledge of the exact number of metastases (see Variant 1).

Several older studies have demonstrated that the dose of intravenous contrast used for MRI is important in determining the number of lesions detected as well as the confidence level associated with the radiologic interpretation. One study reported that high-dose contrast (0.3 mmol/kg gadolinium) is superior in lesion detection without any increase in serious toxicity compared to standard-dose contrast (0.1 mmol/kg gadolinium). However, there is also evidence that the strength of the MRI magnet is important in the ability to detect brain metastases. Another study analyzed the subjective assessment of MRIs done with standard-dose or triple-dose contrast in both 1.5T and 3T magnetic fields. Improved images were obtained with both higher dose of contrast and higher magnet strength. The double-dose concept was introduced using gadolinium. Since then, new contrast media have become available and seems to offer significantly greater diagnostic information and lesion enhancement even at lower doses. Therefore, the concept of double-dose contrast has more or less become obsolete, even with 1.5T magnets, with the availability of the newer contrast agents. (See Variant 2.) Small studies have suggested that other tests such as dynamic contrast-enhanced MRI, perfusion imaging, and MR spectroscopy may help differentiate between brain metastases and high-grade gliomas.

The bulk of the literature regarding the use of brain CT or MRI for staging purposes has dealt with lung cancer. Nevertheless, there is still no general agreement on when to use CT or MRI as part of the initial staging evaluation for a patient newly diagnosed with lung cancer. The decision may vary with the type and stage of lung cancer. One prospective study found that MRI did not change the initial stage of asymptomatic patients with small-cell lung cancer. The only patients found to have asymptomatic brain metastases already had extensive stage disease demonstrated by other tests such as a positive bone scan or liver metastases on CT scan of the abdomen. Although brain MRI appears to be a superior imaging technique compared with brain CT, CT is still widely used as a staging procedure because of its easy accessibility and lower cost. A retrospective study concluded that 10% of patients with otherwise operable NSCLC had brain metastases identified on CT scans of the brain. The absence of neurologic symptoms did not exclude brain metastases since 64% of patients with metastases detected by CT were asymptomatic. Conversely, another study found that CT scans did not reveal unsuspected brain metastases in patients without strong evidence of disseminated disease, such as neurologic signs or symptoms, bone pain, or elevated serum calcium. This study did not address the utility of CT scans in otherwise operable patients, and it is possible that their patient group had a more advanced stage of disease at presentation than that seen in the previous study, which would account for the different conclusions reached by the two studies. A prospective study of brain CT in 105 patients with potentially resectable NSCLC cancer found brain metastases in 4.8% of patients. The authors concluded that the cost savings achieved by avoiding of thoracotomy was far larger than the cost associated with the CT scans.

Positron Emission Tomography

Positron emission tomography (PET) with fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) has been evaluated as a means of identifying brain metastases. PET studies in small numbers of patients have been associated with low sensitivity and specificity rates in the detection of brain metastases. PET scans have also been tested as a means of differentiating various abnormalities already detected by more conventional imaging studies such as CT or MRI. Whole-body FDG-PET is more useful in locating the primary lesion and sites of extracranial metastases in a patient with documented brain metastases. The lack of sensitivity or specificity of cerebral FDG-PET is likely due to the large background of glucose activity within the brain. Alternative tracers to FDG such as 3-deoxy-3-fluorothymidine, thallium-201, or ^{11}C-methionine PET may in the future prove to be more useful in the imaging of brain metastases.

Pathologic Confirmation

Several authors have sought to determine whether histologic confirmation is required following the identification of a suspected solitary metastasis or multiple brain metastases. In one study in which stereotactic biopsy or resection was performed in patients with suspected solitary brain metastasis, 11% of these patients were found to have other tumor histology or lesions of infectious or inflammatory origin. Stereotactic biopsy is equivalent to resection in determining the correct tissue diagnosis in most patients if an appropriate number of biopsies are obtained and confirmation is immediately available by frozen section histology. Although multifocal malignant gliomas are relatively uncommon compared with brain metastases, the two clinical conditions may be difficult to distinguish on the basis of current conventional imaging studies. However, new MRI methods (perfusion and MR spectroscopy) have shown improvement in specificity. Identification of a solitary brain lesion in a patient with a controlled extracranial primary cancer with no other sites of disease on systemic evaluation should be followed by 1) MRI with increased dose of contrast and, if no additional lesions are identified, 2) histologic verification. In patients found to have multiple brain lesions with imaging characteristics compatible with metastases, the decision whether to pursue histological confirmation is based on the clinical picture. Patients with progressive extracranial cancer are seldom subjected to histological confirmation of multiple brain lesions or new solitary lesions.

It is common practice to obtain a neurosurgical opinion regarding surgical intervention to debulk or completely resect brain metastases in a patient presenting with hydrocephalus due to a posterior fossa metastasis or in a patient with impending cerebral or cerebellar herniation from mass effect caused by a bulky brain metastasis.

Steroids

Although clinical experience has established the effectiveness of corticosteroids such as dexamethasone in reducing symptoms and MRI evidence of peritumoral edema, the need for corticosteroids in all patients with brain metastases and the appropriate dose of such medication are points of some research and controversy. One study surveyed 38 oncologists at a single large cancer center who managed patients with brain metastases to document the use of steroids and the frequency of their side effects. Ninety percent of physicians responded to the survey. Fifty-five percent determined the dose of steroid according to the presence or absence of neurological symptoms. The other 45% routinely started 4 mg dexamethasone 4 times a day. Sixty percent tapered the steroid dose in the 4 weeks following completion of whole-brain radiation therapy.

Early studies concluded that patients with newly diagnosed brain metastases should be placed on steroids prior to whole-brain radiation therapy using unconventional radiation dose/fractionation regimens. For example, in one prospective clinical trial in which various whole-brain radiation dose/fraction schedules were used, steroids were started only when there was concern about high intracranial pressure. The results of this study suggest that patients undergoing whole-brain radiation therapy with high doses per fraction should be started on steroids prior to treatment. Twenty-seven percent of patients treated with a single dose of 10 Gy single-fraction whole-brain radiation therapy experienced acute signs or symptoms of increased intracranial pressure. This dose/fractionation of whole-brain radiation therapy is not in common use at this time. Another study, conducted by the Radiation Therapy Oncology Group® nearly two decades ago, found that patients with moderate neurologic signs or symptoms experienced more rapid improvement in their clinical state when radiation treatment was accompanied by steroids. However, steroids did not result in prolongation of progression-free survival or overall survival.

Despite the acknowledged benefits of steroids in reducing edema and alleviating symptoms, the acute and chronic side effects of dexamethasone cannot be ignored. A randomized study comparing dosages of 4, 8, and 16 mg of dexamethasone per day found no advantage to higher dosages compared with 4 mg per day in patients with no evidence of impending herniation. Steroid-related toxicity was more common at the higher doses. There was, however, a trend toward improved performance 28 days after starting dexamethasone in patients on the high doses of steroids. This improvement in the higher dose group was attributed to the early steroid taper in the low-dose group, beginning on the seventh day of cranial irradiation, which led to clinical deterioration in some patients. Based on this observation, the authors of the study recommended 4 mg per day without a dose taper for 28 days in patients without symptoms or signs of mass effect.

A group of investigators studied 138 patients with primary or metastatic brain tumors treated with radiation therapy. Ninety-one patients with brain metastases were treated with standard-fraction whole-brain radiation therapy over 2 to 3 weeks. Most of these patients received dexamethasone

with tapering doses, for a mean duration of 6.9 weeks. Clinical improvements, possibly attributable to dexamethasone, were observed in 33% of patients shortly after it was initiated, in 44% during radiotherapy, and in 11% after radiotherapy. However, side effects possibly attributable to dexamethasone were frequently observed, including hyperglycemia (47%), peripheral edema (11%), psychiatric disorder (10%), oropharyngeal candidiasis (7%), Cushing syndrome (4%), muscular weakness (4%), and pulmonary embolism (2%). Among 13 patients treated without dexamethasone, treatment was well tolerated, except in one patient with brain stem symptoms.

Patients with brain metastases from melanoma and renal cell carcinoma deserve separate considerations. Patients with these cancers are frequently treated with agents such as interleukin-2 (melanoma and renal cell carcinoma), ipilimumab (melanoma), and sunitinib (renal cell carcinoma), whose anticancer efficacy may be lessened when a corticosteroid is taken concurrently. It is crucial that the radiation oncologist communicates with the treating medical oncologist to discuss the pros and cons of using a corticosteroid, especially when the patient is only very mildly symptomatic (see Variant 3).

In summary, there is little compelling evidence to support the routine use of steroids in the newly diagnosed patient with brain metastases who has no neurological signs or symptoms. Likewise, there is no compelling evidence that in the absence of neurological symptoms, steroids should be started simply because the patient is about to start radiation therapy. Steroids cause toxicity, and may mitigate the therapeutic effects of systemic therapy for renal cell carcinoma and melanoma. Therefore, any recommendation for steroids must be rendered in light of this fact. For patients with minimal neurological symptoms the panel recommends either starting with 4 to 8 mg/day, or starting with 16 mg/day but tapering after a few days. In all cases, steroids should be tapered as clinically indicated and tolerated. (See Variant 4.)

Prophylactic Anticonvulsants

Another controversy revolves around the need to initiate prophylactic anticonvulsants in patients with brain metastases. A meta-analysis estimated that 15% of patients with brain metastases present with seizures, and most of them are found to have supratentorial lesions. Patients who present with seizures or who develop seizures during therapy should be started on antiseizure medications. Randomized prospective studies have found no significant reduction in the incidence of first seizures in brain tumor patients placed on prophylactic anticonvulsants. New onset of seizures was experienced by approximately 25% of patients treated with prophylactic anticonvulsants, not significantly different than the percentage of patients experiencing new onset of seizures in the control arm. The meta-analysis concluded that there was no evidence that prophylactic anticonvulsants significantly decreased the incidence of first seizure. In the aggregate, these 12 studies included in the meta-analysis recorded a 26% incidence of seizures at or before brain tumor diagnosis (range, 14% to 51%), and a 19% incidence of seizures after brain tumor diagnosis (range, 10% to 45%). Seizures were more common, both before and after brain tumor diagnosis in patients with primary as compared to metastatic brain tumors. More than 20% of patients had side effects severe enough to warrant a change in or discontinuation of the anticonvulsants. A subsequent randomized study of prophylactic anticonvulsants versus observation reached a similar conclusion regarding the lack of benefit of prophylactic anticonvulsants.

One clinical situation in which a benefit to prophylactic anticonvulsants has been suggested is in the patient with brain metastasis from malignant melanoma. A retrospective study found that prophylactic anticonvulsants in patients with brain metastases from metastatic melanoma reduced the subsequent seizure frequency from 37% to 17%. Possible explanations for the high incidence of seizures in patients with brain metastases from melanoma, as opposed to other histologies, include the tendency for these metastases to be located in the superficial cerebral cortex rather than at the junction between gray and white matter. The above-mentioned meta-analysis did not indicate a significant benefit to anticonvulsants in patients with malignant melanoma brain metastases but concluded that further prospective studies of prophylactic anticonvulsants were warranted in this subgroup. The panel consensus is to not start anticonvulsants prophylactically in patients with brain metastases due to any primary cancer, including melanoma. (See Variant 3 and Variant 4.)

Physicians should also be aware of the potential interaction between anticonvulsants and chemotherapy. Anticonvulsants that induce the P450 system of hepatic metabolism can result in clinically significant reduction of plasma levels of chemotherapies that are metabolized by this system. Anticonvulsants that do not induce this system are available and should be selected if this is a concern.

Summary

- Pretreatment evaluation should determine the number, location, and size of the brain metastases.
- MRI is the recommended imaging technique, particularly in patients being considered for surgery or radiosurgery.
- Contiguous thin-cut volumetric MRI with gadolinium can improve detection of small brain metastases.
- Use of double-dose or triple-dose contrast at the time of MRI may be no longer necessary with the availability of newer gadolinium-based agents.
- A noncontrast scan should accompany the contrast scan to exclude hemorrhage or fat as the cause of the high signal on postcontrast imaging.
- A systemic workup and medical evaluation are important, given that subsequent treatment for the brain metastases will also depend on the

extent of the extracranial disease and the age and performance status of the patient.

- Patients with hydrocephalus or impending brain herniation should be started on high doses of corticosteroids and evaluated for possible neurosurgical intervention.
- Patients with moderate symptoms should receive approximately 4 to 8 mg/day of dexamethasone in divided doses.
- The routine use of corticosteroids in patients without neurological symptoms is not necessary.
- There is no proven benefit of anticonvulsants in the patient who has not experienced seizures.

Abbreviations

- CT, computed tomography
- MRI, magnetic resonance imaging

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Brain metastases

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Neurological Surgery

Neurology

Oncology

Pathology

Radiation Oncology

Radiology

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of radiologic examinations and treatment procedures for pre-irradiation evaluation and management of brain metastases

Target Population

Patients with brain metastases

Interventions and Practices Considered

1. Magnetic resonance imaging (MRI) head
    - With standard-dose contrast
    - With high-dose contrast
2. Computed tomography (CT) head with contrast
3. Corticosteroid therapy
4. Anticonvulsants (prophylactic)

Major Outcomes Considered

- Utility of radiologic examinations in diagnosis of brain metastases
- Sensitivity, specificity, and accuracy of radiologic examinations in detection of brain metastases
- Effectiveness of corticosteroids and anticonvulsants
- Survival (median, overall, seizure-free)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Study Quality Category Definitions

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - There are important study design limitations.

Category 4 - The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:

a. The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description).
b. The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence.
c. The study is an expert opinion or consensus document.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiologic imaging procedures for pre-irradiation evaluation and management of patients with brain metastases

Potential Harms

- Despite the acknowledged benefits of steroids, the acute and chronic side effects of dexamethasone cannot be ignored. In one study, steroid-related toxicity was more common at the higher doses. In another study, side effects possibly attributable to dexamethasone were frequently observed, including hyperglycemia (47%), peripheral edema (11%), psychiatric disorder (10%), oropharyngeal candidiasis (7%), Cushing syndrome (4%), muscular weakness (4%), and pulmonary embolism (2%). Corticosteroids may interfere with efficacy of ipilimumab and interleukin-2.
- Steroids cause toxicity and may mitigate the therapeutic effects of systemic therapy for renal cell carcinoma and melanoma.
- Physicians should be aware of the potential interaction between anticonvulsants and chemotherapy. Anticonvulsants that induce the P450 system of hepatic metabolism can result in clinically significant reduction of plasma levels of chemotherapies that are metabolized by this system.
- In a meta-analysis, more than 20% of patients had side effects severe enough to warrant a change in or discontinuation of anticonvulsants. A study regarding prophylactic anticonvulsants versus observation concluded there was a lack of benefit of prophylactic anticonvulsants.

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1999 (revised 2014)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology-Brain Metastases

Composition of Group That Authored the Guideline

Panel Members: Simon Shek-Man Lo, MB, ChB (*Principal Author*); Elizabeth M. Gore, MD (*Panel Vice-chair*); Jeffrey D. Bradley, MD; John M. Buatti, MD; Isabelle Germano, MD; A. Paiman Ghafoori, MD; Mark A. Henderson, MD; Gregory J. A. Murad, MD; Roy A. Patchell, MD; Samir H. Patel, MD; Jared R. Robbins, MD; H. Ian Robins, MD, PhD; Andrew D. Vassil, MD; Franz J. Wippold II, MD; Michael J. Yunes, MD; Gregory M. M. Videtic, MD (*Panel Chair*)

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Gaspar LE, Videtic GM, Gore EM, Bradley JD, Germano I, Ghafoori P, Henderson MA, Lutz ST, McDermott MW, Patchell RA, Patel SH, Robins HI, Vassil AD, Wippold FJ II, Expert Panel on Radiation Oncology-Brain Metastases. ACR Appropriateness Criteria® pre-irradiation evaluation and management of brain metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 6 p. [36 references]

Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 1 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available from the ACR Web site.
- ACR Appropriateness Criteria® pre-irradiation evaluation and management of brain metastases. Evidence table. Reston (VA): American College of Radiology; 2014. 16 p. Electronic copies: Available from the ACR Web site.

Patient Resources

None available

NGC Status

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